

AMENDMENTS TO THE SPECIFICATION

Please amend the following paragraphs as indicated below. Deletions are indicated with bold double brackets or a simple strikethrough and additions are underlined.

[0021] Another feature of the invention is that the crosslinked polymer compositions have a high compression strength and high swellability, i.e., a composition that has been dried will swell to three times (or more) its dried size upon rehydration, and is more "elastic." Since these polymers are generally very hydrophilic, they are more easily injected, i.e., the crosslinked composition stays as a "cohesive mass" when injected through a fine ~~gague~~ gauge (27-30 gauge) needle.

[0035] wherein $[m > 2, n > 2, \text{ and } m + n > 5]$ $m \geq 2, n \geq 2, \text{ and } m + n \geq 5;$

[0037] $[[Y = -\text{CO}_2\text{N}(\text{COCH}_2)_2]]$ $Y = -\text{CO}_2\text{N}(\text{COCH}_2)_2$, $-\text{CO}_2\text{H}$, $-\text{CHO}$, $-\text{CHOCH}_2$, $-\text{N}=\text{C}=\text{O}$, $[[\text{SO}_2\text{CH}=\text{CH}_2]]$ $-\text{SO}_2\text{CH}=\text{CH}_2$, $-\text{N}(\text{COCH}_2)_2$, $-\text{S}-\text{S}-(\text{C}_5\text{H}_4\text{N})$, etc., and can be the same or different; and

[0043] $[[\text{CH}_2\text{CH}_2\text{O}]_n-]$ $-(\text{CH}_2\text{CH}_2\text{O})_n-$ or $-(\text{CH}(\text{CH}_3)\text{CH}_2\text{O})_n-$ or $-(\text{CH}_2\text{CH}_2\text{O})_n - (\text{CH}(\text{CH}_3)\text{CH}_2\text{O})_n-$.

[0051] $[[-\text{O}_2\text{C}-(\text{CH}_2)_n-]]$ $-\text{O}_2\text{C}-(\text{CH}_2)_n-$ polymer - $\text{O}_2\text{C}-(\text{CH}_2)_n-\text{X}$ (or Y)

[0061] $[[\text{polymer} - \text{NH}-\text{OCH}_2\text{CH}_2\text{CO} - \text{polymer}]]$ $\text{polymer} - \text{NH}-\text{OCH}_2\text{CH}_2\text{CO} - \text{polymer}$

[0082] Various forms of multi-amino PEG are commercially available from Nektar ~~Therapeutics~~ Therapeutics, Inc. of San Carlos, CA (through its acquisition of Shearwater Polymers of Huntsville, AL), and from Texaco Chemical Company of Houston, TX under the name "Jeffamine." Multi-amino PEGs useful in the present invention include Texaco's Jeffamine diamines ("D" series) and triamines ("T" series), which contain two and three primary amino groups per molecule, respectively. General structures for the Jeffamine diamines and triamines are shown in Figure 3.

[0083] Polyamines such as ethylenediamine $[(\text{H}_2\text{N}-\text{CH}_2\text{CH}_2-\text{NH}_2)]$ $(\text{H}_2\text{N}-\text{CH}_2\text{CH}_2-\text{NH}_2)$, tetramethylenediamine $[(\text{H}_2\text{N}(\text{CH}_2)_3\text{NH}_2)]$ $(\text{H}_2\text{N}(\text{CH}_2)_4\text{NH}_2)$, pentamethylenediamine (cadaverine) $(\text{H}_2\text{N}-(\text{CH}_2)_5-\text{NH}_2)$, hexamethylenediamine $[(\text{H}_2\text{N}-(\text{CH}_2)_6-\text{NH}_2)]$ $(\text{H}_2\text{N}-(\text{CH}_2)_6-\text{NH}_2)$, bis(2-hydroxyethyl)amine $[(\text{HN}-(\text{CH}_2\text{CH}_2\text{OH})_2)]$ $(\text{HN}-(\text{CH}_2\text{CH}_2\text{OH})_2)$, bis(2-aminoethyl)amine (HN-

(CH₂CH₂NH₂)₂), and tris(2-aminoethyl)amine (N-(CH₂CH₂NH₂)₃) may also be used as the synthetic polymer containing multiple nucleophilic groups.

[0099] As discussed above, preferred activated polyethylene glycol derivatives for use in the invention contain succinimidyl groups as the reactive group. However, different activating groups can be attached at sites along the length of the PEG molecule. For example, PEG can be derivatized to form functionally activated PEG ~~propion-aldehyde~~ propionaldehyde (A-PEG), the tetrafunctionally activated form of which is shown in Figure 10, as is the conjugate formed by the reaction of A-PEG with multi-amino PEG. The linkage shown in Figure 10 is referred to as a -(CH₂)_m-NH- linkage, where m = 1 - 10.

[0105] Many of the activated forms of polyethylene glycol described above are now available commercially from Nektar ~~Therapeutics~~ Therapeutics and Union Carbide of South Charleston, W.V.

[0115] Polyamines such as ethylenediamine [(H₂N-CH₂ CH₂-NH₂)] (H₂N-CH₂CH₂-NH₂), tetramethylenediamine (H₂N-(CH₂)₄NH₂), pentamethylenediamine (cadaverine) [(H₂N-(CH₂)₅-NH₂)] (H₂N-(CH₂)₅-NH₂), hexamethylenediamine [(H₂N-(CH₂)₆-NH₂)] (H₂N-(CH₂)₆-NH₂), bis(2-hydroxyethyl)amine [(HN-(CH₂CH₂OH)₂)] (HN-(CH₂CH₂OH)₂), bis(2-aminoethyl)amine [(HN-(CH₂CH₂NH₂)₂)] (HN(CH₂CH₂NH₂)₂), and tris(2-aminoethyl)amine (N-(CH₂CH₂NH₂)₃) can be chemically derivatized to polyacids, which can then be derivatized to contain two or more succinimidyl groups by reacting with the appropriate molar amounts of N-hydroxysuccinimide in the presence of DCC, as described in U.S. Patent No. 5,580,923. Many of these polyamines are commercially available from DuPont Chemical Company.

[0135] Chemically modified collagens[[.]] that are in nonfibrillar form at neutral pH include succinylated collagen and methylated collagen, both of which can be prepared according to the methods described in U.S. Patent No. 4,164,559, issued August 14, 1979, to Miyata et al., which is hereby incorporated by reference in its entirety. Due to its inherent tackiness, methylated collagen is particularly preferred for use in bioadhesive compositions, as disclosed in commonly owned U.S. Patent No. 5,614,587.